REMARKS

The Applicants have amended Claims 1, 2, 3, 7, 9, 10, 12, 17, 18, 21, 23, and 26 and cancelled Claim 22. Thus, Claims 1-3, 5-7, 9-19, 21, and 23-27 are presented for examination. The specific changes to the amended claims are shown above in the Amendments to the Claims, wherein the insertions are underlined and the ~~deletions are stricken through~~. The Applicants respond below to rejections and objections raised by the Examiner in the Office Action of August 29, 2003.

I. Rejections under 35 U.S.C. § 103

Claims 1-2, 6, and 12-13 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Kastan *et al.* (US 6,387,640 B1) in view of Rappold *et al.* JCB Vol. 153(3), pp. 613-620. The Applicants respectfully submit that these claims are not rendered obvious by the prior art of record.

The Examiner acknowledges that Kastan *et al.* do not teach the use of ATM deficient cells for ATM expression. The Examiner alleges, however, that it would have been obvious to use ATM deficient cells as taught by Rappold *et al.* in carrying out the cloning methods of Kastan *et al.* The Applicants respectfully submit, however, that the results of the presently claimed method were unexpected and surprising because the process generates ATM protein in quantities that were previously unattainable. Specifically, the use of a variola viral vector (and in particular a vaccinia viral vector) has been shown to produce high yields of ATM protein as described in the specification. See, *e.g.*, page 11, line 4 to page 12, line 2; page 20, lines 10-19.

Prior to the present invention, methods of producing ATM yielded very small quantities of ATM compared with expected yields based on experience with the expression of other proteins. As discussed in the specification, the best prior art attempt to overexpress ATM in transfected cells produced only 1 μg from a 225 cm^2 flask that had been seeded with 8 x 10^6 cells. See page 3, lines 13-22.

Although Kastan *et al.* state that a vaccinia virus can be used as a viral vector when expressing ATM, it is only one vector in a list of many preferred viral vectors. To a person of ordinary skill in the art, Kastan *et al.* provides no motivation to select vaccinia virus in particular. Finally, even if Kastan *et al.* were to be combined with the other prior art of record for a teaching

of expression of ATM in ATM deficient mammalian cells, there would be no expectation of success on the magnitude of the present invention. The Applicants respectfully submit, therefore, that the claims are not rendered obvious.

Claims 1-2, 6, 15, 17, 19, and 21 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Kastan *et al.* (US 6,387,640 B1) in view of Zhang et al. PNAS 94, pp. 8021-8026. The Applicants respectfully submit that these claims are not rendered obvious by the prior art of record.

As above, the Examiner acknowledges that Kastan *et al.* do not teach the use of ATM deficient cells for ATM expression. The Examiner alleges, however, that it would have been obvious to use ATM deficient cells as taught by Zhang *et al.* in carrying out the cloning methods of Kastan *et al.* For the reasons discussed above, the Applicants respectfully submit, that the results of the presently claimed method were unexpected and surprising because the process generates ATM protein in quantities that were previously unattainable. Further, there would have been no motivation to use vaccinia virus particularly as in the present invention. Accordingly, the Applicants respectfully submit that the present claims are not rendered obvious.

In view of the above, the Applicants respectfully request that the § 103 rejections be withdrawn and the pending claims allowed over the art of record.

II. Rejections under 35 U.S.C. § 112

Claims 1-3, 5-7, 9-19, and 21-27 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement.

The Examiner has alleged that the Applicants do not disclose the claimed gene and instead disclose only cDNA. The Applicants respectfully submit that the specification states that the ATM gene is disclosed at GenBank Accession No. U82828 (Platzer *et al.* (1997) *Genome Res.* 7 (6) 592-605) and ATM mRNA is disclosed at GenBank Accession No. U33841 (Savitsky *et al.* (1995) *Hum. Mol. Genet.* 4: 2025-2032). See page 2, lines 1-7. Nevertheless, the Applicants have amended the claims so that they now refer to a "cDNA encoding the ATM protein" rather than a "gene encoding the ATM protein."

Claims 1-3, 5-7, 9-19, and 21-27 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claims the subject matter which applicant regards as the invention.

The Examiner has alleged that certain claims are vague for reciting the term "ATM protein." The Applicants respectfully submit, however, that the specification identifies ATM protein as a 350 kDa protein kinase that is encoded by the A-T gene; the gene is disclosed at GenBank Accession No. U82828 (Platzer *et al.* (1997) *Genome Res.* 7 (6) 592-605) and ATM mRNA is disclosed at GenBank Accession No. U33841 (Savitsky *et al.* (1995) *Hum. Mol. Genet.* 4: 2025-2032). See page 1, line 26 to page 2, line 7. The Applicants note that "ATM" stands for "ataxia-telangiectasia mutated" and recognize that the name is somewhat misleading since the ATM protein is generally considered normal and healthy by those of skill in the art at the present time. The use of the term "mutated" in connection with this protein is merely a product of the scientific discovery process as the protein was at one time thought to be abnormal. The Applicants respectfully submit that those of skill in the art will interpret the term "ATM protein" as having a definition consistent with its use in the present specification.

The Examiner has further alleged that certain claims are vague for reciting the term "functional ATM protein." The Applicants respectfully submit, however, that the term "functional" as applied to a protein means that the protein is capable of performing one or more of its ordinary functions. For example, one function of ATM protein that is recited in the specification is the detection of double strand DNA breaks. See page 5, lines 30-31. In some embodiments, "functional" ATM protein would be able perform that detection function under appropriate conditions. The Applicants respectfully submit that those of skill in the art will understand the term "functional" as applied to a protein and will correspondingly understand the term "functional ATM protein."

The Examiner has rejected Claim 7 as being unclear as to whether the HeLa cells are ATM deficient. The Applicants submit that Claim 7, in its amended form, makes clear that the HeLa cells are ATM deficient.

The Examiner has rejected Claim 10 for reciting the limitation "said ATM deficient cells." The Applicants have amended this claim to recite "said ATM deficient mammalian cells" as the Examiner has recommended.

The Examiner has rejected Claim 17 for reciting the relative term "high yield." This claim has now been amended so that the term "high yield" has been removed. Instead, the claim

now recites a numerical threshold relating to the yield, namely "2 μg substantially purified ATM protein per 300 grams fresh weight of mammalian cells."

The Examiner has rejected Claim 22 as being unclear with respect to the isolation using an antibody specific for the FLAG epitope. The Applicants submit that this claim has been cancelled and that the rejection is now moot.

CONCLUSION

The Applicants have endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. Accordingly, amendments to the claims, the reasons therefor, and arguments in support of the patentability of the pending claim set are presented above. Any claim amendments which are not specifically discussed in the above remarks are made in order to improve the clarity of claim language, to correct grammatical mistakes or ambiguities, and to otherwise improve the capacity of the claims to particularly and distinctly point out the invention to those of skill in the art. In light of the above amendments and remarks, reconsideration and withdrawal of the outstanding rejections is respectfully requested. If the Examiner has any questions which may be answered by telephone, she is invited to call the undersigned directly.

Respectfully submitted,
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